

General

Guideline Title

Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients.

Bibliographic Source(s)

Jacobi J, Bircher N, Krinsley J, Agus M, Braithwaite SS, Deutschman C, Freire AX, Geehan D, Kohl B, Nasraway SA, Rigby M, Sands K, Schallom L, Taylor B, Umpierrez G, Mazuski J, Schunemann H. Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. Crit Care Med. 2012 Dec;40(12):3251-76. [222 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The grades of evidence (High, Moderate, Low, Very Low) and levels of recommendations (Strong, Weak) are defined at the end of the "Major Recommendations" field. Strong recommendations are listed as "recommendations" and weak recommendations as "suggestions."

Note: While the initial goal was to suggest glycemic targets for critically ill patients, the limited available literature has narrowed the scope of this article and the ability to make recommendations for specific populations. An overriding focus is on the safe use of insulin infusions. The glycemic goal range of 100–150 mg/dL is a consensus goal, and while it differs slightly from the more stringent goal of 110–140 mg/dL for selected populations, recently published by the American Diabetes Association, and the overall glucose goal of 140–180 mg/dL, this difference is not likely to be clinically significant.

1. In adult critically ill patients, does achievement of a blood glucose (BG) <150 mg/dL with an insulin infusion reduce mortality, compared with the use of an insulin infusion targeting higher BG ranges?

The task force suggests that a BG \geq 150 mg/dL should trigger initiation of insulin therapy, titrated to keep BG <150 mg/dL for most adult intensive care unit (ICU) patients and to maintain BG values absolutely <180 mg/dL using a protocol that achieves a low rate of hypoglycemia (BG \leq 70 mg/dL) despite limited impact on patient mortality. [Quality of evidence: very low]

2. In adult critically ill patients, what are the morbidity benefits of maintaining BG <150 mg/dL?
 - A. The task force suggests that there is no consistently demonstrated difference in several morbidity measures (renal failure, transfusion, bacteremia, polyneuropathy, and ICU length of stay [LOS]) when evaluated in the general adult ICU population. [Quality of evidence: very low]
 - B. The task force suggests implementation of moderate glycemic control (GC) (BG <150 mg/dL) in the postoperative period following cardiac surgery to achieve a reduced risk of deep sternal wound infection and mortality. [Quality of evidence: very low]

- C. In the population of critically ill injured (trauma) ICU patients, the task force suggests that BG ≥ 150 mg/dL should trigger initiation of insulin therapy, titrated to keep BG < 150 mg/dL for most adult trauma patients and to maintain BG values absolutely < 180 mg/dL, using a protocol that achieves a low rate of hypoglycemia (BG ≤ 70 mg/dL) to achieve lower rates of infection and shorter ICU stays in trauma patients. [Quality of evidence: very low]
 - D. The task force suggests that a BG ≥ 150 mg/dL triggers initiation of insulin therapy for most patients admitted to an ICU with the diagnoses of ischemic stroke, intraparenchymal hemorrhage, aneurysmal subarachnoid hemorrhage, or traumatic brain injury (TBI), titrated to achieve BG values absolutely < 180 mg/dL with minimal BG excursions < 100 mg/dL, to minimize the adverse effects of hyperglycemia. [Quality of evidence: very low]
 - E. The task force further suggests that BG < 100 mg/dL be avoided during insulin infusion for patients with brain injury. [Quality of evidence: very low]
3. What is the impact of hypoglycemia in the general ICU population?

The task force suggests that BG ≤ 70 mg/dL are associated with an increase in mortality, and that even brief severe hypoglycemia (SH) (BG ≤ 40 mg/dL) is independently associated with a greater risk of mortality and that the risk increases with prolonged or frequent episodes. [Quality of evidence: low]
 4. How should insulin-induced hypoglycemia be treated in adult ICU patients?

The task force suggests that BG < 70 mg/dL (< 100 mg/dL in neurologic injury patients) be treated immediately by stopping the insulin infusion and administering 10–20 g of hypertonic (50%) dextrose, titrated based on the initial hypoglycemic value to avoid overcorrection. The BG should be repeated in 15 mins with further dextrose administration as needed to achieve BG > 70 mg/dL with a goal to avoid iatrogenic hyperglycemia. [Quality of data: very low]
 5. How often should BG be monitored in adult ICU patients?

The task force suggests that BG be monitored every 1–2 hrs for most patients receiving an insulin infusion. [Quality of evidence: very low]
 6. Are point-of-care (POC) glucose meters accurate for BG testing during insulin infusion therapy in adult ICU patient?

The task force suggests that most POC glucose meters are acceptable but not optimal for routine BG testing during insulin infusion therapy. Clinicians must be aware of potential limitations in accuracy of glucose meters for patients with concurrent anemia, hypoxia, and interfering drugs. [Quality of evidence: very low]
 7. When should alternatives to fingerstick capillary sampling be used in adult ICU patients?

The task force suggests arterial or venous whole blood sampling instead of finger-stick capillary BG testing for patients in shock, on vasopressor therapy, or with severe peripheral edema, and for any patient on a prolonged insulin infusion. [Quality of evidence: moderate]
 8. Can continuous glucose monitoring replace POC methods for critically ill patients?

In the absence of compelling data, no recommendation can be made for or against the use of continuous glucose sensors in critical care patients. [Quality of evidence: very low]
 9. How should intravenous (IV) insulin be prepared and administered?

The task force suggests continuous insulin infusion (1 unit/mL) therapy be initiated after priming new tubing with a 20-mL waste volume. [Quality of evidence: moderate]
 10. What is the role for subcutaneous (SQ) insulin in adult ICU patients?

Subcutaneous insulin may be an alternative treatment for selected ICU patients. [Quality of evidence: very low]
 11. How should adult ICU patients be transitioned off IV insulin infusions?
 - A. The task force suggests that stable ICU patients should be transitioned to a protocol-driven basal/bolus insulin regimen before the insulin infusion is stopped to avoid a significant loss of GC. [Quality of evidence: very low]
 - B. The task force suggests that calculation of basal and bolus insulin dosing requirements should be based on the patient's IV insulin infusion history and carbohydrate intake. [Quality of evidence: very low]
 12. What are the nutritional considerations with IV insulin therapy in adult ICU patients?
 - A. The task force suggests that the amount and timing of carbohydrate intake should be evaluated when calculating insulin requirements. [Quality of evidence: low]
 - B. The task force also suggests that GC protocols should include instructions to address unplanned discontinuance of any form of carbohydrate infusion. [Quality of evidence: low]
 13. What factors should be considered for safe insulin therapy programs in the adult ICU?

The task force suggests that insulin is a high-risk medication, and that a systems-based approach is needed to reduce errors. [Quality of evidence: very low]

14. What are the characteristics of an optimal insulin dosing protocol for the adult ICU population?

The task force suggests that ICUs develop a protocolized approach to manage GC. Components include a validated insulin administration protocol, appropriate staffing resources, use of accurate monitoring technologies, and a robust data platform to monitor protocol performance and clinical outcome measures. A standard insulin infusion protocol should include a requirement for continuous glucose intake, standardized IV insulin infusion preparation, a dosing format requiring minimal bedside decision-making, frequent BG monitoring, provisions for dextrose replacement if feedings are interrupted, and protocolized dextrose dosing for prompt treatment of hypoglycemia. [Quality of evidence: very low]

15. What is the impact of glycemic variability (GV) on outcomes of critically ill patients?

GV has been independently associated with mortality in several cohorts of critically ill patients; however, there is no consensus regarding the appropriate metric for mathematically defining GV. The task force suggests that the simplest tools—standard deviation (SD) of each patient's mean BG and coefficient of variation (SD/mean)—be reported in all published interventional studies. [Quality of evidence: very low]

16. What metrics are needed to evaluate the quality and safety of an insulin infusion protocol and GC program in the adult ICU?

Measures of overall glucose control should include mean (SD) and median (IQR) BG levels as well as ICU-level run charts of percentage BG <150 mg/dL and 180 mg/dL. The task force suggests that hypoglycemic events should be monitored regularly and reported as events per patient, as a percentage of all BG values, and events per 100 hrs of insulin infusion. [Quality of evidence: very low]

17. What are the economic and workforce impacts of a GC program in the adult ICU?

- A. The task force recommends that programs to monitor and treat hyperglycemia in critically ill patients be implemented to reduce hospital costs. [Quality of evidence: moderate]
- B. The task force suggests implementation of programs to monitor and treat hyperglycemia in diabetic patients following cardiovascular surgery to reduce hospital costs. [Quality of evidence: low]

18. What are the implications of hyperglycemia in pediatric critically ill patients?

In the absence of compelling data, no recommendations could be made for or against the use of tight GC in pediatric critical care patients.

Definitions:

Grades of Evidence

Grade A (High): Randomized controlled trial (RCT)

Grade B (Moderate): Downgraded RCT or upgraded observational studies

Grade C (Low): Well-done observational studies with control RCTs

Grade D (Very Low): Downgraded controlled studies or expert opinion based on other evidence

Strength of Recommendations

Grade 1 (Strong): A recommendation in favor of an intervention reflects that the desirable effects of adherence to a recommendation (beneficial health outcomes, less burden on staff and patients, and cost savings) will clearly outweigh the undesirable effects (harms, more burden and greater costs).

Grade 2 (Weak): A recommendation in favor of an intervention indicates that the desirable effects of adherence to a recommendation probably will outweigh the undesirable effects, but the panel is not confident about these tradeoffs – either because some of the evidence is low-quality (and thus there remains uncertainty regarding the benefits and risks) or the benefits and downsides are closely balanced.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Hyperglycemia

Guideline Category

Management

Treatment

Clinical Specialty

Critical Care

Endocrinology

Internal Medicine

Intended Users

Advanced Practice Nurses

Health Care Providers

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To evaluate the available literature and address aspects of implementation that permit safe and effective insulin infusion therapy
- To help clinicians achieve the blood glucose (BG) goal that is considered to have the greatest benefit and safety for their patient population while avoiding clinically significant hypoglycemia
- To discuss intravenous (IV) insulin therapy primarily, while subcutaneous (SQ) administration may also have a role for glycemic control (GC) in stable intensive care unit (ICU) patients

Note:

Other agents and approaches, including oral hypoglycemic drugs, and other antidiabetic agents may be continued or restarted in selected patients, but will not be discussed in this article. Studies evaluating insulin as a component of other therapies (such as glucose–insulin–potassium) were not evaluated.

Nutritional support requirements of critically ill patients vary and are beyond the scope of this discussion.

Target Population

Adult medical and surgical intensive care unit (ICU) patients

Note: Data on the glycemic management of pediatric ICU patients are limited, but will be described where available.

Interventions and Practices Considered

1. Frequent monitoring of blood glucose levels
2. Insulin protocol
 - Intravenous
 - Subcutaneous
3. Standardized approaches to infusion preparation
4. Consistent intake of nutrition
5. Dextrose replacement
6. Systems-based approach

Major Outcomes Considered

- Mortality
- Morbidity
- Prevention and detection of hypoglycemia (blood glucose ≤ 70 mg/dL)
- Glycemic variability
- Safety and effectiveness of insulin infusion therapy

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Applicable literature was compiled using a variety of search engines (PubMed, OVID, Google Scholar, reference lists from other publications, search of Clinicaltrials.gov, and the expertise and experience of the authors). Searches were performed periodically until the end of 2010 using the following terms: acute stroke, BG, cardiac surgery, critical care, critical illness, critically ill patients, dextrose, glucose, glucose control, glucose metabolism, glucose meters, glucose toxicity, glycemic control, glycemic variability, hyperglycemia, hypoglycemia, ICU, insulin, insulin infusion, insulin protocols, insulin resistance, insulin therapy, intensive care, intensive insulin therapy, mortality, myocardial infarction, neurocognitive function, neuroprotection, outcomes, pediatric, pediatric intensive care, point-of-care, point-of-care testing, sepsis, sternal wound infection, stress hyperglycemia, stress, stress hormones, stroke, subarachnoid hemorrhage, surgery, tight glycemic control protocols, and traumatic brain injury (TBI).

Published clinical trials were used as the primary support for guideline statements, with each study evaluated and given a level of evidence. Abstracts and unpublished studies or data were not included in the analysis.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grades of Evidence

Grade A (High): Randomized controlled trial (RCT)

Grade B (Moderate): Downgraded RCT or upgraded observational studies

Grade C (Low): Well-done observational studies with control RCTs

Grade D (Very Low): Downgraded controlled studies or expert opinion based on other evidence

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to rate the quality of evidence and strength of the recommendation for each clinical practice question. A member of the GRADE group was available to provide input and answer methodologic questions.

Meta-analyses using RevMan and GRADEPro software were applied to organize evidence tables, create forest and funnel plots, and draw conclusions about the overall treatment effects or specific outcomes applicable to a particular recommendation.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Recommendations are classified as strong (Grade 1) or weak (Grade 2) and are focused on specific populations where possible. Strong recommendations are listed as "recommendations" and weak recommendations as "suggestions." Throughout the development of the guidelines, there was an emphasis on patient safety and whether the benefit of adherence to the recommendation would outweigh the potential risk, the burden on staff, and when possible, the cost. If the risk associated with an intervention limited the potential for benefit, or if the literature was not strong, the statement was weakened to a suggestion. Individual patient or intensive care unit (ICU) circumstances may influence the applicability of a recommendation. It is important to recognize that strong recommendations do not necessarily represent standards of care.

Numerous discussions among the authors led to consensus regarding the recommendations. Individual members or subgroups drafted the recommendations and justifications. Subsequently, each recommendation was reviewed by the Task Force members who were provided the opportunity to comment, propose changes, and approve or disapprove each statement. Once compiled, each member was again asked to review the article and provide input. Consensus was sought for recommendation statements, and controversial statements were repeatedly edited and feedback provided through secret ballots until there was consensus.

Rating Scheme for the Strength of the Recommendations

Levels of Recommendations

Grade 1 (Strong): A recommendation in favor of an intervention reflects that the desirable effects of adherence to a recommendation (beneficial health outcomes, less burden on staff and patients, and cost savings) will clearly outweigh the undesirable effects (harms, more burden and greater costs).

Grade 2 (Weak): A recommendation in favor of an intervention indicates that the desirable effects of adherence to a recommendation probably will

outweigh the undesirable effects, but the panel is not confident about these tradeoffs – either because some of the evidence is low-quality (and thus there remains uncertainty regarding the benefits and risks) or the benefits and downsides are closely balanced.

Cost Analysis

The guideline developer reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

External peer review was provided through the Critical Care Medicine editorial process, and approval was obtained by the governing board of the Society of Critical Care Medicine.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Glycemic control (GC) that can be accomplished safely and with justifiable utilization of resources
- Prevention of hypoglycemia in critically ill patients
- Increased patient safety

Potential Harms

- Glycemic control (GC) can be difficult to manage. Glycemic variability may contribute to adverse outcomes.
- Over/under correction of blood glucose may occur.
- Hypoglycemia carries specific risks for the normal brain and a greater risk for the injured brain. Severe hypoglycemia (SH) can produce or exacerbate focal neurological deficits, encephalopathy, seizures or status epilepticus, permanent cognitive dysfunction, and death. Further, tight GC may induce regional neuroglycopenia in traumatic brain injury (TBI).
- While the first priority is patient safety through restoration of normoglycemia, rebound hyperglycemia due to excessive replacement should also be avoided, especially because the resulting increase in glycemic variability (GV) may contribute to adverse outcomes.

Qualifying Statements

Qualifying Statements

Guidelines are limited by the available literature and the expertise of the writing panel and reviewers. The recommendations are not absolute

requirements, and therapy should be tailored to individual patients and the expertise and equipment available in a particular intensive care unit (ICU). The use of an insulin infusion requires an appropriate protocol and point-of-care (POC) monitoring equipment with frequent blood glucose (BG) monitoring to avoid hypoglycemia. Recommendations may not be applicable to all ICU populations, and limitations will be discussed when applicable. Future literature may alter the recommendations and should be considered when applying the recommendations within this article.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Jacobi J, Bircher N, Krinsley J, Agus M, Braithwaite SS, Deutschman C, Freire AX, Geehan D, Kohl B, Nasraway SA, Rigby M, Sands K, Schallom L, Taylor B, Umpierrez G, Mazuski J, Schunemann H. Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. *Crit Care Med*. 2012 Dec;40(12):3251-76. [222 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Dec

Guideline Developer(s)

Society of Critical Care Medicine - Professional Association

Source(s) of Funding

Society of Critical Care Medicine (SCCM)

Guideline Committee

Society of Critical Care Medicine Guideline Task Force

Composition of Group That Authored the Guideline

Authors: Judith Jacobi, PharmD, FCCM; Nicholas Bircher, MD, FCCM; James Krinsley, MD, FCCM; Michael Agus, MD; Susan S. Braithwaite, MD; Clifford Deutschman, MD, FCCM; Amado X. Freire, MD, MPH, FCCM; Douglas Geehan, MD, FCCM; Benjamin Kohl, MD, FCCM; Stanley A. Nasraway, MD, FCCM; Mark Rigby, MD, PhD, FCCM; Karen Sands, APRN-BC, ANP, MSN, CCRN; Lynn Schallom, RN, MSN, CCNS, FCCM; Beth Taylor, MS, RD, CNSD, FCCM; Guillermo Umpierrez, MD; John Mazuski, MD, PhD, FCCM; Holger Schunemann, MD

Financial Disclosures/Conflicts of Interest

Dr. Agus has consulted for the Diabetes Technology Society. He also has a pending patent on an extracorporeal membrane oxygenation (ECMO)-based glucose sensor, which is not connected to idea discussed in this article. Dr. Braithwaite has a U.S. patent. Dr. Kohl has received grant support from Amlyn and Eli Lilly. Dr. Krinsley has performed consulting work for Medtronic Inc., Edwards Life Sciences, Baxter, Roche Diagnostics, and Optiscan Biomedical and has received speaker's fees from Edwards Life Sciences, Roche Diagnostics and Sanofi-Aventis. Dr. Nasraway has consulted for Optiscan, Echo Therapeutics. Dr. Geehan has received grant support from the Department of Defense Research. Dr. Rigby has received consulting fees from Medtronic. Dr. Schallom has received honoraria/speaking fees from Roche Laboratories Speakers Bureau on Glycemic Control. The remaining authors have not disclosed any potential conflicts of interest.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [Society of Critical Care Medicine \(SCCM\) Web site](#)

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Print copies: Available from the Society of Critical Care Medicine, 500 Midway Drive, Mount Prospect, IL 60056; Phone: (847) 827-6869; Fax: (847) 827-6886; on-line through the [SCCM Bookstore](#) .

Availability of Companion Documents

The following is available:

- New glycemic control guidelines. Podcast. 2012. Available from the [Society of Critical Care Medicine Web site](#) .
Also available through the [iTunes Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on May 15, 2013. The information was verified by the guideline developer on June 17, 2013.

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